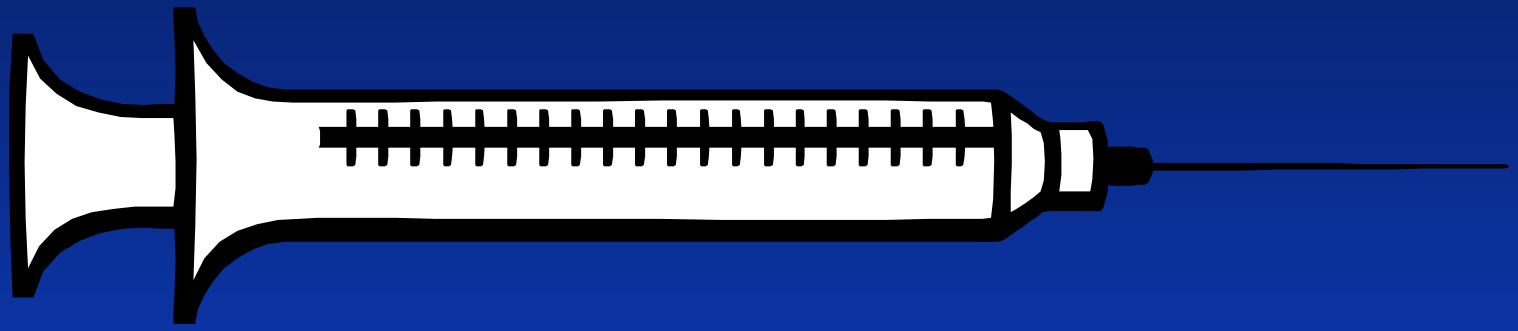
Vaccine Preventable Diseases



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Vaccines
Who gets what?

- **Routine**
  - diphtheria/tetanus (DPT for children)
  - polio (IPV or OPV)
  - MMR (measles, mumps, rubella)
- **Travelers**
  - yellow fever (Africa and South America)
  - typhoid
  - hepatitis A
  - meningococcus
  - Japanese encephalitis (> 4 weeks in endemic areas of Asia)
  - rabies (> 4 weeks in areas with canine rabies)
- **Special**
  - hepatitis B (sexually active travelers
  - pneumococcus
  - Hemophilus influenzae B
  - adenovirus
  - BCG
  - anthrax
  - smallpox

$1.90

Diphtheria/Tetanus Vaccines

- **Type: adsorbed toxins**
- **Indications: universal; DPT or DT to children, dT to adults. Increased incidence of diphtheria in Eastern Europe.**
- **Efficacy: > 90%**
- **Precautions**
  - **hypersensitivity to previous doses**
  - **previous severe local reaction**

Diphtheria/Tetanus Vaccines

Dosing schedule for patients > 7 yo

- **Primary**
  - **2 doses of 0.5 ml IM at least 4 weeks apart**
  - **3rd dose of 0.5 ml IM 6 - 12 weeks after 2nd**
- **Booster**
  - **every 10 years**
  - **new recommendations for adults from the ACIP are one dose after age 50, if primary series already completed**
- **Side Effects**
  - **mild local reactions and fever**
  - **multiple recent doses may induce an Arthus reaction.**

Polio
Going the way of smallpox?

- An enteroviral disease spread by food, water, or person-to-person
- Wild polio has been eradicated from the entire Western Hemisphere but still occurs in Africa, Asia, the Mideast, and Eastern Europe

  Summer 2000 outbreak of vaccine strain that has regained virulence and caused > 20 cases in the Dominican Republic and Haiti
- Vaccine is recommended universally.
  - Primary series is 4 doses of OPV (live attenuated) or IPV (inactivated).
  - Boosters are recommended for children and adults traveling to high-risk areas.

    one dose of IPV or OPV beyond primary series

Polio Vaccine

$17.05

- Inactivated vaccine (IPV) is not associated with any cases of paralytic disease, while OPV carries a 1:2.4 million chance.

- Previously unvaccinated adults, immunocompromised (or household contact) should only receive IPV (0.5 mL sub cut in the deltoid) to reduce chances of paralytic disease
  - OPV is no longer indicated (or available) in the US for children or adults due to risk of paralytic disease
  - Summer 2000 in Haiti & Dom Rep - development of paralytic polio from an OPV strain that regained virulence

MMR

$18.84

Measles, Mumps, Rubella

- **Type: live attenuated strains of all 3 viruses**
- **Indications: universal**
- **Efficacy: > 95%**
- **Precautions**
  - **Pregnancy**
  - **Severe immunosuppression (HIV is not a contraindication)**
  - **Anaphylaxis to egg ingestion and to neomycin**

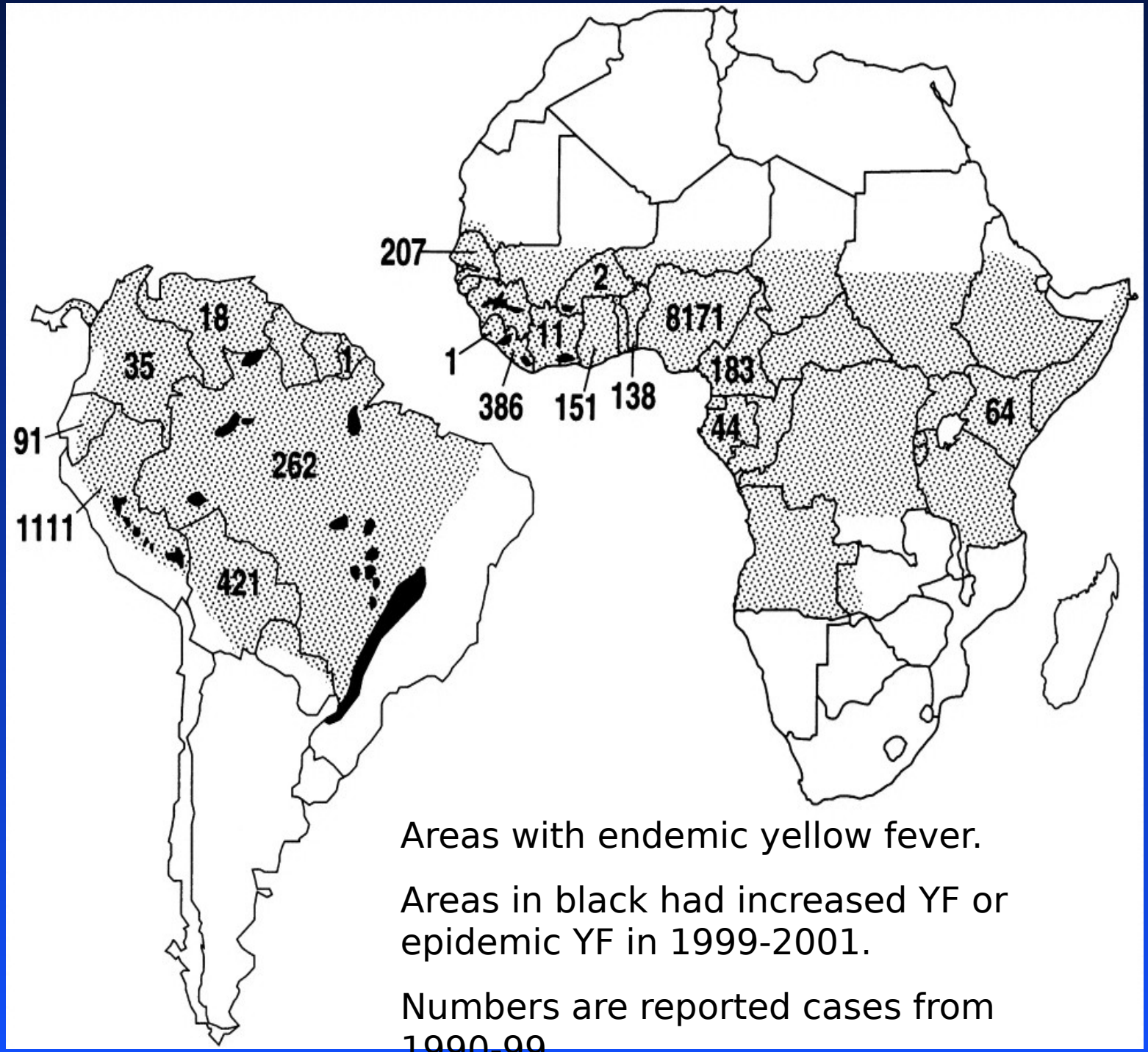
Measles
Vaccines

- **Development of measles vaccine in the early 60's resulted in a 99% reduction in US cases.**
- **Recent resurgence in the US and a continued major killer in the developing world**

  4 - 22% of US measles cases are linked to intl travel.
- **Many Americans born after 1957 may not be immune.**

  One dose of vaccine will seroconvert > 95%, the remaining 5% are able to maintain the infection in the population.

  Some may have obtained the less effective, inactivated vaccine available from 1963-67.



Areas with endemic yellow fever.

Areas in black had increased YF or epidemic YF in 1999-2001.

Numbers are reported cases from 1990-99

Yellow Fever Vaccine

$47.07

- Type: Live attenuated virus
  - (multiple passages in chick embryonic tissue in 1936)
- Indications: Travel to endemic areas of South America and Africa (not Asia)
- Efficacy: Near 100%
- Precautions
  - immunocompromised
  - anaphylaxis to eggs
  - avoid in pregnancy if possible
  - contraindicated in children < 4 months, relatively so in ages 4 - 9 months

Monath CID 2002;34:1369-78

Yellow Fever in Travelers, 1970-2000

Date of Dx	Age in years, sex	Vaccination status	Place of residence	Place of exposure	Outcome
October 1979	42, M	Not vaccinated	France	Senegal	Died
October 1979	25, M	Not vaccinated	France	Senegal	Died
August 1985	27, F	Not vaccinated	The Netherlands	Guinea-Bissau, The Gambia, Senegal	Survived
October 1987	37, F	Vaccinated	Spain	Niger, Mali, Burkina Faso, Mauritania	Survived
April 1996	53, M	Not vaccinated	Switzerland	Brazil	Died
August 1996	42, M	Not vaccinated	United States	Brazil	Died
August 1999	40, M	Not vaccinated	Germany	Ivory Coast	Died
September 1999	48, M	Not vaccinated	United States	Venezuela	Died

Yellow Fever
Vaccine

- **Dosage: 0.5 ml subcutaneously (adults and children)**
- **Booster: once every 10 years (may be lifelong)**
- **Side effects:**
  - **2 - 5%: Mild local and systemic effects occur 5 - 10 days after vaccination.**
  - **Extremely rare: encephalitis/encephalopathy, especially in infants**

Typhoid Vaccine

Three types available:

Oral Vaccine Ty 21a

- **mutant, attenuated strain given as four doses on alternating day regimen.**
- **must refrigerate and dose on an empty stomach without hot fluids**
- **poor patient compliance**
- **cannot be used with concurrent antibiotics or mefloquine**
- **booster q 5 years**

Parenteral Polysaccharide Vi Antigen Vaccine **$24.85**

- **fewer local side effects than the old phenol or heat inactivated whole bacteria vaccines**
- **single initial dose with booster q 2 years**

Table 19. Dosage and schedules for typhoid fever vaccination

		Dosage			+
Vaccination	**Age**	**Dose/mode of administration**	**Number of Doses**	**Interval Between Doses**	**Boosting Interval**
Oral live-attenuated Ty21a vaccine					
Primary series	≥ 6 yrs	1 capsule*	4	48 hrs	—
Booster	≥ 6 yrs	1 capsule*	4	48 hrs	every 5 yrs
Vi capsular polysaccharide vaccine					
Primary series	≥ 2 yrs	0.50 mL†	1	—	—
Booster	≥ 2 yrs	0.50 mL†	1	—	every 2 yrs
Heat-phenol-inactivated parenteral vaccine					
Primary series	6 mos–10 yrs ≥ 10 yrs	0.25 mL§ 0.50 mL§	2 2	≥ 4 wks ≥ 4 wks	— —
Booster	6 mos-10 yrs ≥10 yrs ≥6 mos	0.25 mL§ 0.50 mL§ 0.10 mL¶	1 1 1	— — —	every 3 yrs every 3 yrs every 3 yrs

*Administer with cool liquid no warmer than 37° C (98.6° F).

†Intramuscularly.

§Subcutaneously.

¶Intradermally.

—Not applicable.

Table 20. Common adverse reactions to typhoid fever vaccines

	Reactions		
Vaccine	**Fever**	**Headache**	**Local Reactions**
Ty21a*	0%–5%	0%–5%	Not applicable
ViCPS	0%–1%	1.5%–3%	Erythema or induration ≤ 1 cm: 7%
Parenteral inactivated	6.7%–24%	9%–10%	Severe local pain or swelling: 3%–35%

*The side effects of Ty21a are rare and mainly consist of abdominal discomfort, nausea, vomiting, and rash or urticaria.

Meningococcus $57.49

Meningococcal Meningitis

- ***Neisseria meningitidis*: common pediatric infection (typically < 5 yo) prevalent with crowding (ie. bootcamp, barracks, ships, etc.)**
- **Most carriers do not develop illness, may transmit infections ~ 6 months.**
- **Serogroups**
  - **most endemic/epidemic disease in Africa is group A**
  - **most epidemic disease in S. America is group B**
  - **most sporadic disease in N. America is group B and C**
- **Sub-Saharan "meningitis belt" extends from Senegal and Guinea in the west to Ethiopia in the east.**

Meningococcal Disease in DoD

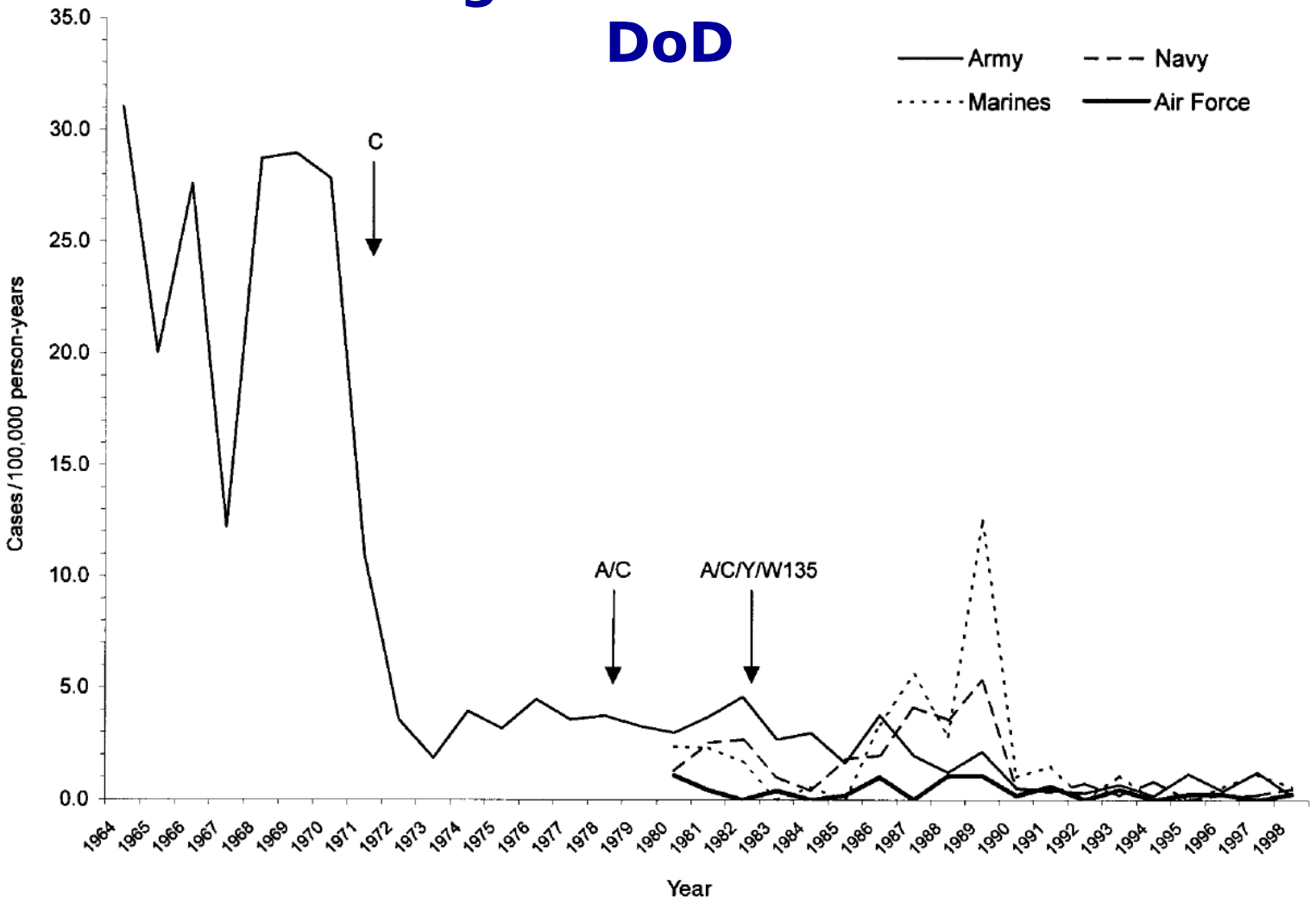
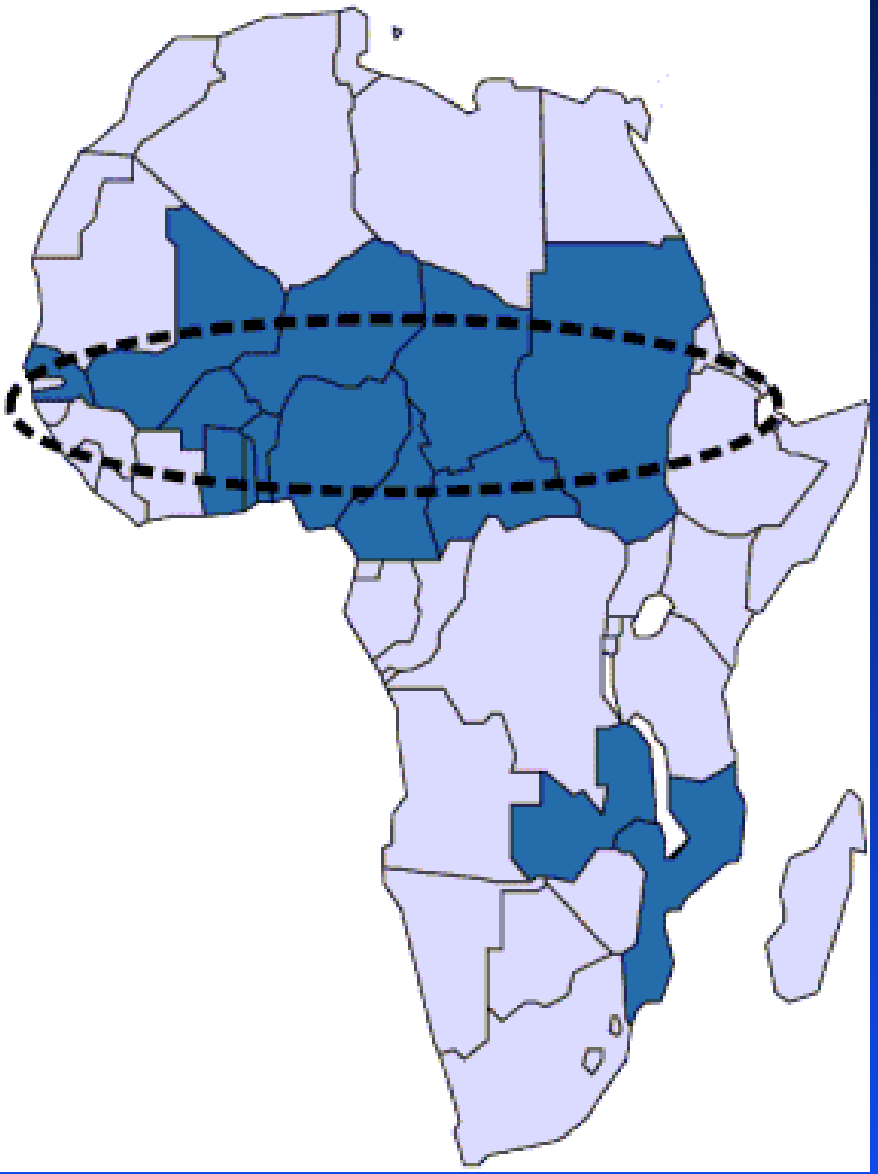


Figure 1. Rates of meningococcal disease among active-duty members of the US Armed Forces in relation to routine uses of meningococcal vaccines with various serogroup-specific components, 1964–1998. Arrows indicate dates of initiation of routine use of various vaccines.

Brundage et al. CID 2002; 35:1376–81

Meningitis belt

Countries reporting more than 15 cases per 100 000 population and an epidemic of meningococcal disease from January 1995 to October 1999



WHO Report on Global Surveillance of Epidemic-prone Infectious Diseases - 2001

Meningococcus
Vaccine

- **85 - 90% efficacious polysaccharide, inactivated-bacterial vaccine against serogroups A, C, Y, W-135. *Menomune***
- **No currently available vaccine for group B disease**
  - **Polyvalent vaccines with above five serogroups investigational**
- **Indicated for all asplenic patients**
- **Travelers to Africa and epidemic areas should consider vaccine especially in December thru June.**
  - **Required for Saudi Arabia**
- **Primary series: 0.5 cc subcutaneously ~ 2 weeks before travel. Booster q 3 - 5 years**
  - **Mild erythema at site is only side effect in adults. Up to 2% of children may have transient fever.**

Meningococcus
Conjugate Vaccine

- ***Menactra*** **aproved by FDA Sep 04**
- **Quadrivalent A,C.Y. W-135**
- **More immunogenic**
  - **British study documented 85% decrease in cases and 90% decrease in deaths**
  - **60% decrease in Non immunized (herd immunity)**
- **? More prolonged immune response**
- **Expensive!**

Japanese Encephalitis

Description

A flavivirus endemic throughout Asia transmitted by mosquitoes through pigs and wading birds

- most common encephalitis in Asia, exposure universal in childhood
- risk highest in rural areas, especially if pigs are present
- in temperate regions, usually more common in warm months
- locals get disease as children, travelers at any age; very rare in travelers, < 1 case per million; only 11 Americans infected in the last 20 years, but 8/11 were DOD personnel or family
- only ~ 1 in 1,000 infections in Asians are associated with clinical disease, but if sx occur death or serious sequelae are the rule

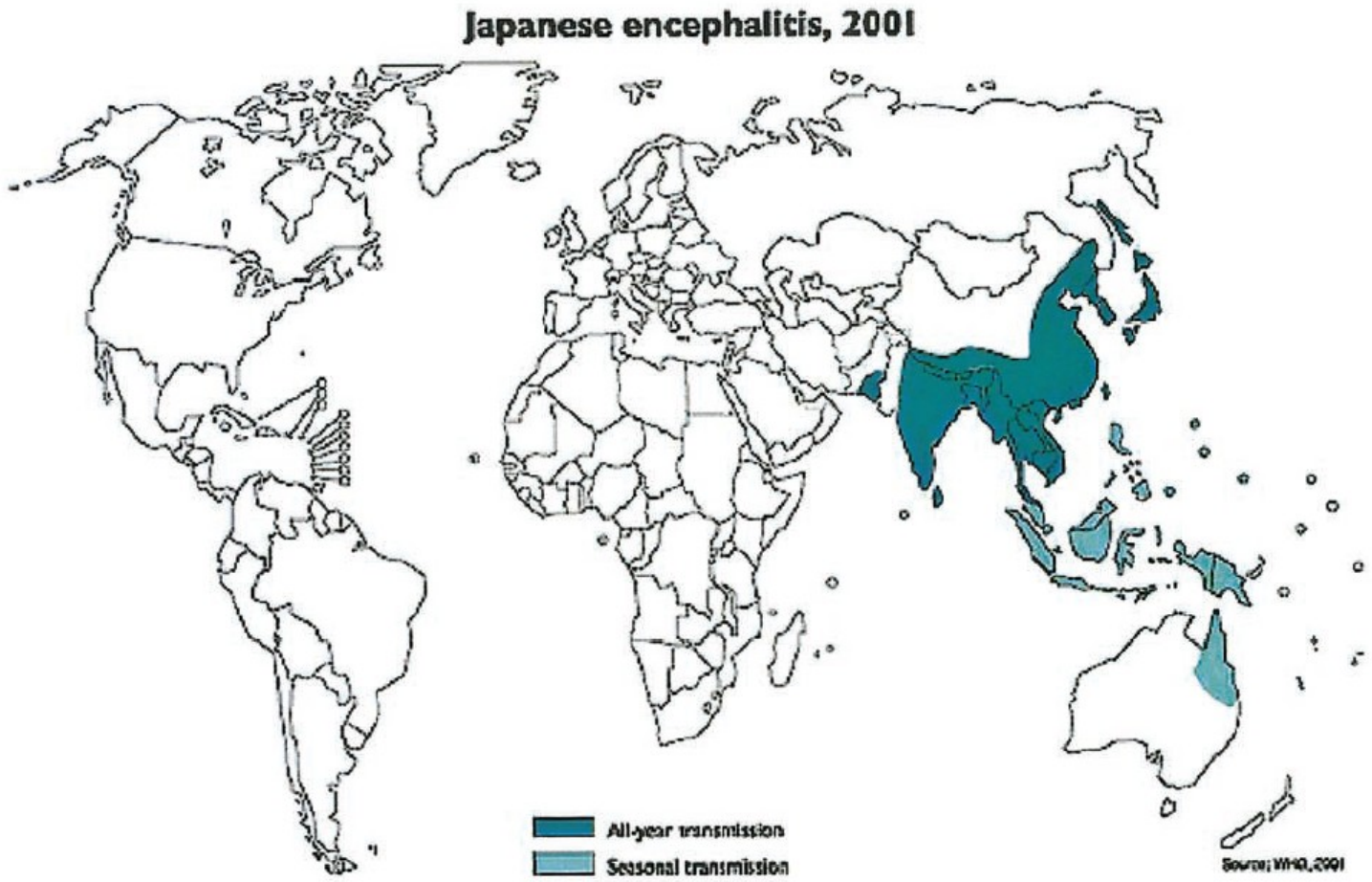


Figure 3. Worldwide distribution of cases of Japanese encephalitis B. Source: World Health Organization. Available at http://www.who.int.

Japanese Encephalitis$60.74

Vaccine

- **Vaccine indicated only for those spending > 30 days in rural areas.**
  - **Most visitors to primarily urban areas do not need vaccine.**

- **Inactivated virus derived from infected mouse brain**
  - **1.0 cc subcutaneously on days, 0, 7, and 30**
  - **If needed, third dose may be given at 14 days.**
  - **80% have immunity after 2nd dose.**
  - **booster doses at 2 - 3 years after primary series**

- **Local side effects in 20% and systemic side effects in 1-% of vaccinees**
  - **1 in 260 develop urticaria or angioedema, rarely anaphylaxis.**
  - **use cautiously if atopic hx, especially *Hymenoptera* sp.**

Rabies
Vaccine

- **Human rabies is common in many developing countries.**
- **Frequency of canine cases is directly correlated with human cases, but cats, cattle, bats, and other animals are often rabid.**
  - **6.8% of street dogs in Thailand are rabid.**
  - **A dog lick was experienced by 8.9% and a dog bite by 1.3% of travelers visiting for an average of 17 days.**
- **Vaccine not indicated for travelers unless staying in rural areas for > 4 weeks or with no access to medical attention.**

  Pre-exposure vaccine for military unit not necessary if ready access to vaccine in the event of exposure.

Rabies Vaccine

- Many inferior vaccines available
  - Often less immunogenic, poorly purified
  - greater association with neurologic and other side effects
- In the US three inactivated vaccines, each nearly 100% efficacious
  - HDCV - Human Diploid Cell Vaccine, from infected human cell line
  - RVA - Rabies Vaccine Absorbed, from diploid cell line derived from fetal rhesus lung cells
  - PCEC - Purified Chick Embryo Cell Culture, if hypersensitivity to one of the above, chicken allergy does not preclude use
- HRIG - Human Rabies Immune Globulin - from vaccinated veterinary students, provides 3 - 6 weeks of passive immunity

$74.23

$96.39 per 2 mL vial

Rabies
Vaccine

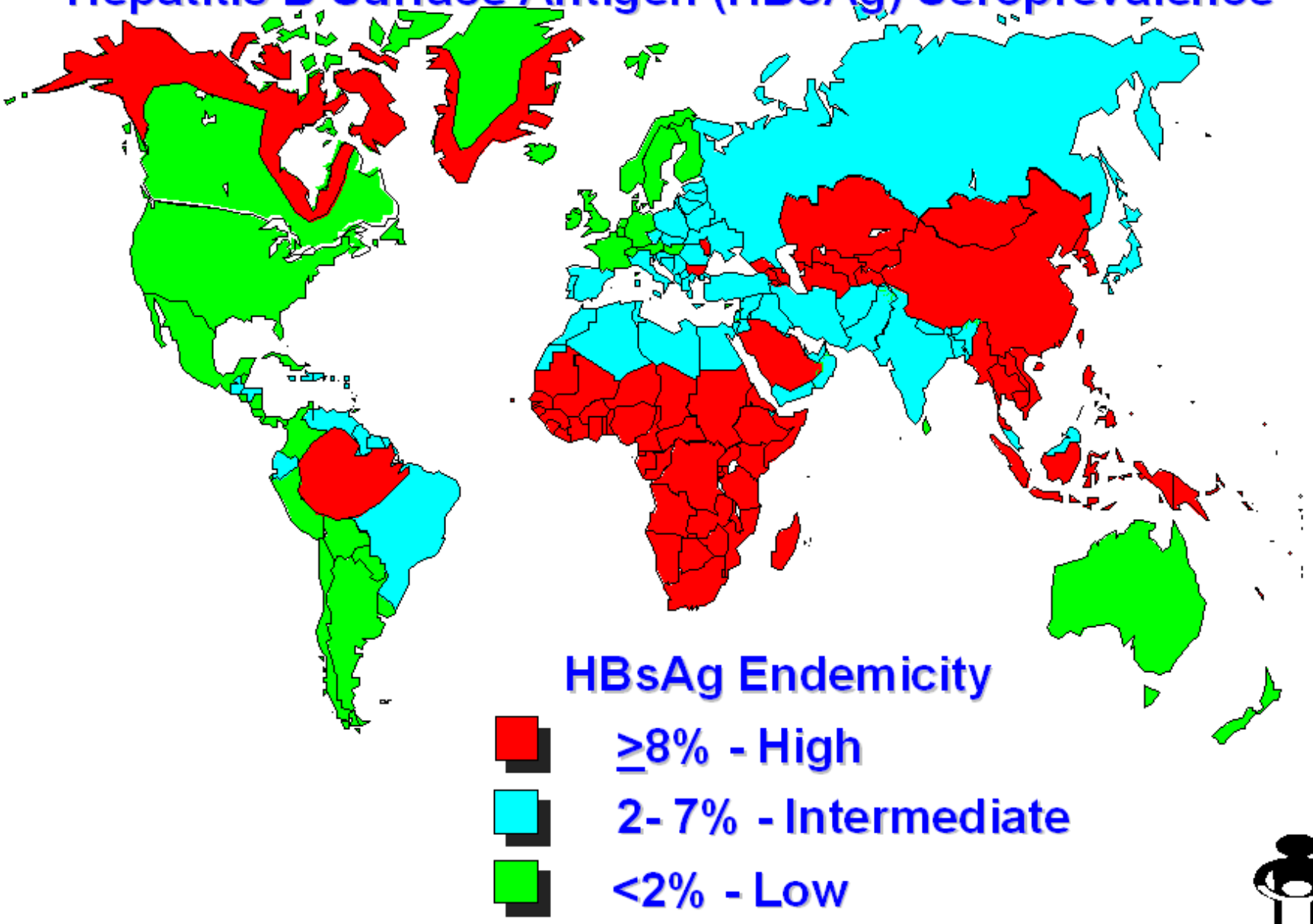
- **Pre-exposure**
  - 1.0 cc IM or 0.1 cc ID in the deltoid
  - days 0, 7, and 21 or 28, complete > 30 days before exposure risk
  - frequent risk give booster q 2 years
  - continuous, high risk, check Ab q 6 m
- **Postexposure**
  - **Clean** the wound and give tetanus booster.
  - If preimmunized, give 1.0 cc deltoid IM on days 0 and 3.
  - If unimmunized give:
    - 20 IU/kg HRIG, half around the site and half in the buttock
    - 1.0cc deltoid IM on days 0, 3, 7, 14, and 28
- **Side effects**
  - Injection site swelling and pain, itching, HA, myalgias and fever may occur.
  - Immune complex reactions occur 2 - 21 days later
    - 6% HDCV
    - 1% RVA booster patients.

Hepatitis A Vaccine

$26.15

- **Live vaccine: either over attenuated and non-immunogenic or under attenuated and pathogenic.**
- **Two inactivated vaccines available in the US**
  - **HAVRIX**
  - **VAQTA**
- **Regimen: two dose 1.0cc deltoid IM either vaccine**
  - **Standard is immunization at 0 and 6-12 months**
  - **DoD recommendations are for all hands during bootcamp**
- **Protective antibodies are present at 2 weeks in >90% after 1st dose**
- **>95% have protective antibody levels after 2nd vaccination**

Geographic Pattern of Hepatitis B Surface Antigen (HBsAg) Seroprevalence



Hepatitis B
Vaccine

- Universal for newborns
- Healthcare workers
- Dialysis patients
- Household contacts of acute and chronic cases
- Sexually promiscuous hetero- and homosexuals
- IVDAs
- Inmates of correctional facilities

Hepatitis B
Prevention Post Exposure

- **Infants born to HBsAg+ mothers or in close contact with HBsAg+ persons**
- **Exposure to HBsAg+ blood**
- **Sexual partners of HBsAg+ individuals,** if given within two weeks of exposure

Hepatitis B
Vaccine

$23.50 adult

$6.10 peds

- **All the vaccines currently available in the US are recombinant, inactivated viral antigen.**
- **Schedule for adults is 1 cc deltoid IM at 0, 1, and 6 months.**
- **Side effects are common but mild and usually limited to soreness at injection site, fatigue, headache, and nausea.**
- **Contraindicated if hypersensitive to yeast.**
- **Failure to seroconvert should prompt boosting up to 3 doses.**
- **Interval for boosters in those with initial Ab response is unknown (10 years?).**

Pneumococcal Disease $5.94

Pneumovax

- **Disease caused by *Streptococcus pneumoniae* is responsible for deaths of > 40,000 Americans per year.**
- **Generally not considered a predeployment vaccine**
- **Pneumococcal pneumonia is common throughout the world.**
  - **In temperate climates especially in winter and early spring**
  - **outbreaks not common, but often associated with crowding**
- **Increasing resistance worldwide will make the use of vaccine more important.**

Pneumococcal Disease

Pneumovax

- **23-valent inactivated bacterial vaccine**
- **Indicated for**
  - **> 65 yo (some rec > 55 yo)**
  - **any age with chronic conditions: cardiopulmonary disease, diabetes, alcoholism, cirrhosis, persistent CSF leaks**
  - **functional or anatomic asplenia**
- **0.5 mL IM or subcutaneously with booster q 5 - 6 years**
- **Side effects are uncommon, usually local pain and redness.**
  - **Fever myalgias or severe local reactions are rare.**
  - **No increase in side effects with booster doses.**

$38.09

Pneumococcus

Conjugate Vaccines

- Conjugate heptavalent vaccine (*Prevnar*)
- Immunogenic in children <2 yo
  - ≤6 months old: 2,4,6 and 12-15 months
  - 7-11 months old: 2 doses at least 4 weeks apart, third dose after 1 yo
  - 12-23 months old: 2 doses at least 2 months apart
  - >24 months old: 1 dose (if immunocompromised 2 doses)
- $58 per dose in 2002

Hemophilus influenzae $12.06

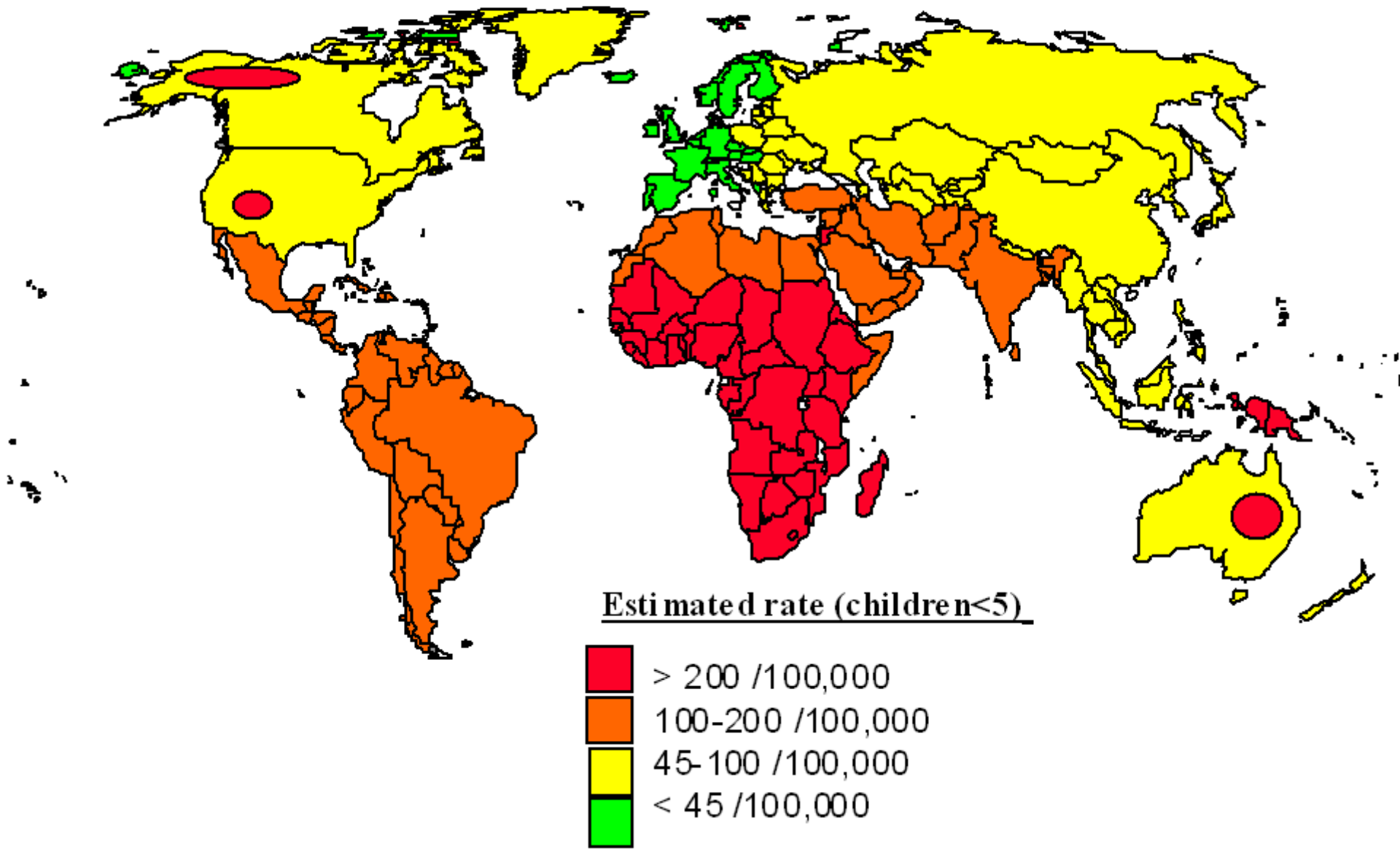
Hib

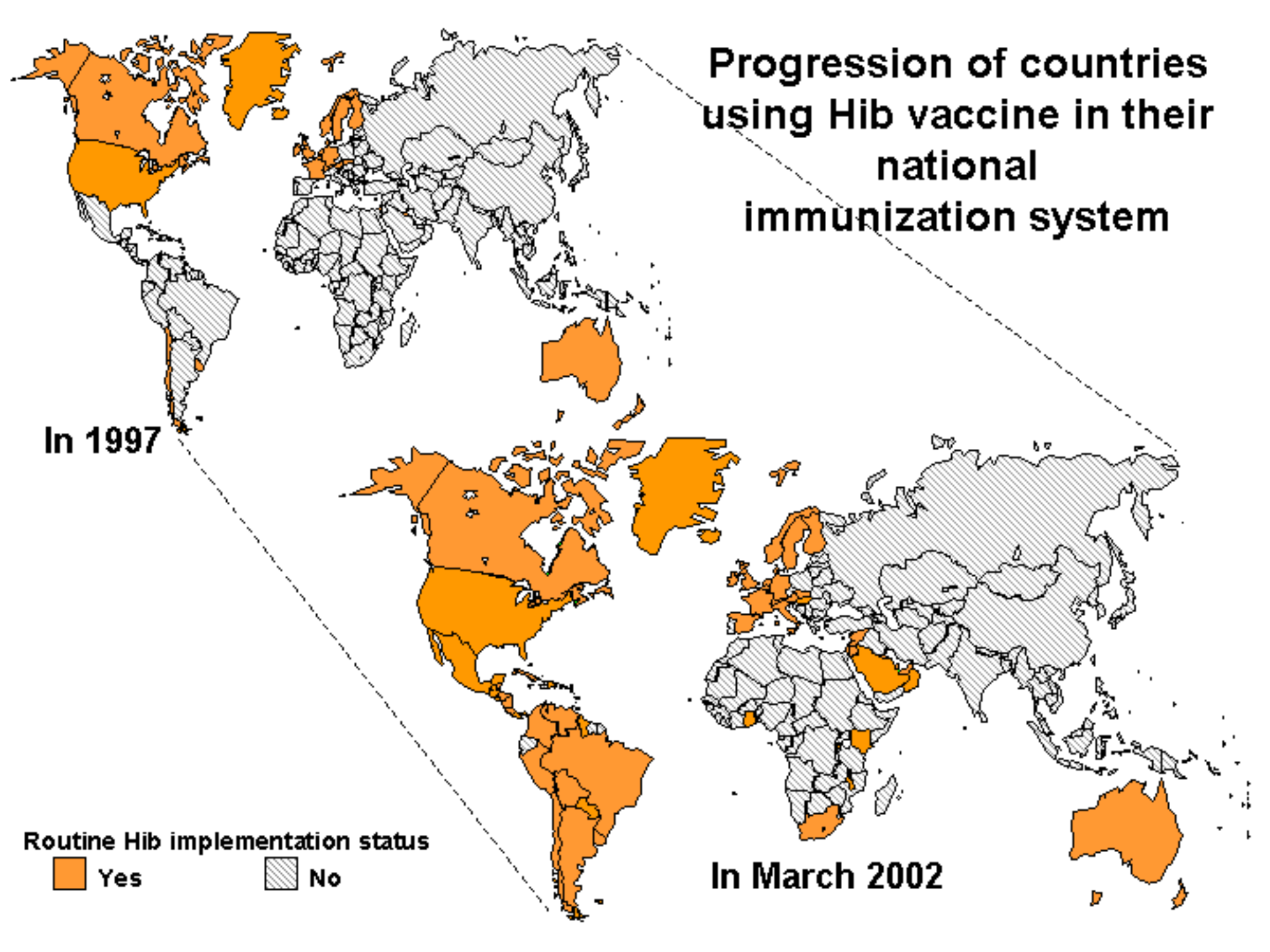
- ***Hemophilus influenzae*: gram negative coccobacillus with six distinct capsular types**
  - **Type B is most often associated with invasive disease.**
  - **Introduction of vaccine decreased invasive *Hib* by > 95%.**

- **Vaccine**
  - **Inactivated bacterial vaccine conjugated to a protein carrier to increase immunogenicity:**

    tetanus toxoid, diphtheria toxoid, *Neisseria meningitidis* protein complex
  - **universal immunization of children with 3 - 4 doses**
  - **only indications in adults are for asplenic individuals and ?HIV-infected**

Estimated rate of Hib meningitis and pneumonia




Progression of countries using Hib vaccine in their national immunization system
In 1997
In March 2002
Routine Hib implementation status
Yes
No

Varicella
Chicken Pox

- ***Varicella zoster virus*** **(VZV): ~ four million US cases of chicken pox per year**
  - **9,300 hospitalizations and 50 - 100 deaths annually**
- **Complications: bacterial superinfection of skin lesions, pneumonia, dehydration, encephalitis, and hepatitis**
  - **Adolescents, adults, pregnant, and immunocompromised do worse**
- **Incubation 10 - 21 days, contagious two days prior to rash and for a few days after onset of rash, but continues until lesions are crusted over**

Varicella Vaccine

$34.45

Varivax

Vaccine: live attenuated virus with excellent efficacy

- **Indications are for all children > 12 months old as one dose; if > 12 yo given in two doses separated by 4 - 8 weeks.**
- **Mild fever, soreness, and erythema are common. A mild VZV infection with a few vesicles may occur rarely and is contagious.**
- **18/100,000 children later developed zoster, but all cases were mild.**
- **Is a booster needed?**

Plague
Vaccine

- Formalin-killed, whole cell vaccine
- No longer routine part of DoD vaccine program
- Efficacy never proven
  - No vaccinated Americans developed plague in WWII and only eight cases reported during the Vietnam War, suggests efficacy
  - Unknown efficacy against inhalational plague (i.e. BW agent or person-to-person from pneumonic cases)

Plague

Next year's Biowarfare agent?

Plague Vaccine

- **Current indications are only for those with:**
  - **Significant rodent exposure in endemic areas, plague lab workers, medical staff caring for plague patients**
  - **not indicated for travelers or residents of endemic areas**
  - **Currently NOT AVAILABLE**

- **Schedule**
  - **3-dose series: 1st dose 1.0 cc IM, 2nd dose 0.2 cc IM 1 - 3 months after 1st dose, and 3rd dose 0.2 cc IM 5 - 6 months after 2nd dose**
  - **Booster: Give 0.2 cc IM q 6 months after above, then q 1 - 2 years for those remaining at risk.**

- **Side Effects**
  - **Local erythema, induration, malaise, headache, adenopathy, and fever are common.**
  - **Nausea, myalgias, arthralgias, and leukocytosis are rare.**
  - **Side effects are more common in those vaccinated repeatedly.**

Tick-Borne Encephalitis
Vaccine

- **A viral infection of the CNS associated with *Ixodes* ticks in Europe and Asia (esp old USSR)**
- **A killed virus vaccine and immune globulin is available in Europe.**
  - **series of three vaccines over a six month period**
  - **considered for DoD use in former Yugoslavia**
  - **IND product not yet FDA approved**

Cholera
Vaccine

- Rarely seen in travelers, risk estimated at 1 in 500,000
- Type: phenol-inactivated suspension of *V. cholerae*
- Indications: only if required by local regulations (currently no countries or territories)
- Efficacy: 50-60% effective against 01 strain for 3-6m
- Precautions
  - not approved for use during pregnancy
  - Avoid in those with previous serious reactions
- No longer available in the US

Cholera
Parenteral Vaccine

- **Dosage**

  Primary series of 2 doses given 1 - 4 weeks (or more) apart

  - **6 m - 4 yo: 0.2 ml sc or im**
  - **5 - 10 yo: 0.3 ml sc or im**
  - **> 10 yo: 0.5 ml sc or im**

- **Booster**

  Repeat dose every 6 months in an endemic area.

- **Side Effects: Very Common**
  - **1 - 2 days of pain, erythema, and induration at the site**
  - **associated with fever, malaise, and headache**

Cholera
Vaccine

- **New oral B subunit vaccines proven effective but not approved in the US.**
  - **–subunit vaccines are also effective against diarrhea caused by ETEC**
- **Since cholera is easily treated with inexpensive oral antibiotics, it is doubtful a drug company will sponsor the expense of FDA approval for US use.**

Borrelia burgdorferi
LYMErix: The Lyme Disease Vaccine

- **Genetically engineered vaccine with lipoprotein OspA**
- **Efficacy Rates**
  - **78% against definite Lyme disease**
  - **100% against asymptomatic infection**
- **Three doses on 0, 1, and 12 month schedule**
- **No longer marketed**

Anthrax

Pathogenesis - Pulmonary Infections

Airborne spores 2 - 5 microns are deposited in alveoli.

- **phagocytized by alveolar macrophages, transported to mediastinal nodes where they multiply and cause hemorrhagic mediastinitis (but not a true pneumonia)**
- **frequently associated with bacteremia**

Anthrax
Clinical Manifestations

Inhalation

- early diagnosis nearly impossible
- early symptoms are “flu-like,” with myalgias, fever, malaise
- dramatically sicker in 2 - 3 days, with severe dyspnea and hypoxemia
  - wide mediastinum and pleural effusions
- progresses to hypotension, 1/2 develop hemorrhagic meningitis (Gram stain and culture of CSF +)
- virtually invariably fatal despite massive antibiotic use

Anthrax Vaccine

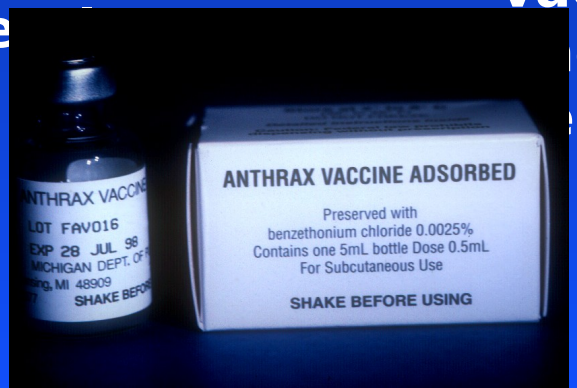
- Has been used for abattoir and textile workers for > 30 years.
- US vaccine is a killed, cell-free filtrate of the PA component of the exotoxin.
- Russian and veterinary vaccines are a live attenuated (unencapsulated) anthrax spore available for > 60 years.
- Concern over use of anthrax spores as a BW agent has heightened military interest.

Anthrax Vaccine

- **US vaccine efficacy against cutaneous anthrax is ~ 92%.**
  - **Efficacy against inhalational disease in humans is ?.**
  - **35% of recipients had at least a mild local reaction.**
    - **2.4% significant local reactions 1st dose, 2.7% subsequent doses**
    - **0.7% systemic reactions 1st dose, 1.3% subsequent doses**
- **Animal studies against aerosolized exposure have shown excellent protective efficacy in primate models.**

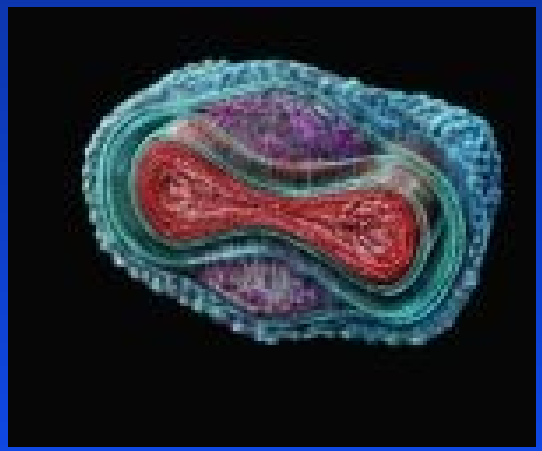
Anthrax Vaccine

- Dosing schedule is complex and based on efficacy trial in humans done over 30 years ago.
- Currently recommended dosing schedule is for 0.5 cc subcutaneously at 0, 2, and 4 weeks and at 6, 12, and 18 months, followed by ye
  boosters.



- Primate studies show probable protection against inhalational anthrax after two doses.
- A highly purified, minimally reactogenic, recombinant protective antigen vaccine using alum
  d other adjuvants is
  ing studied.

Smallpox



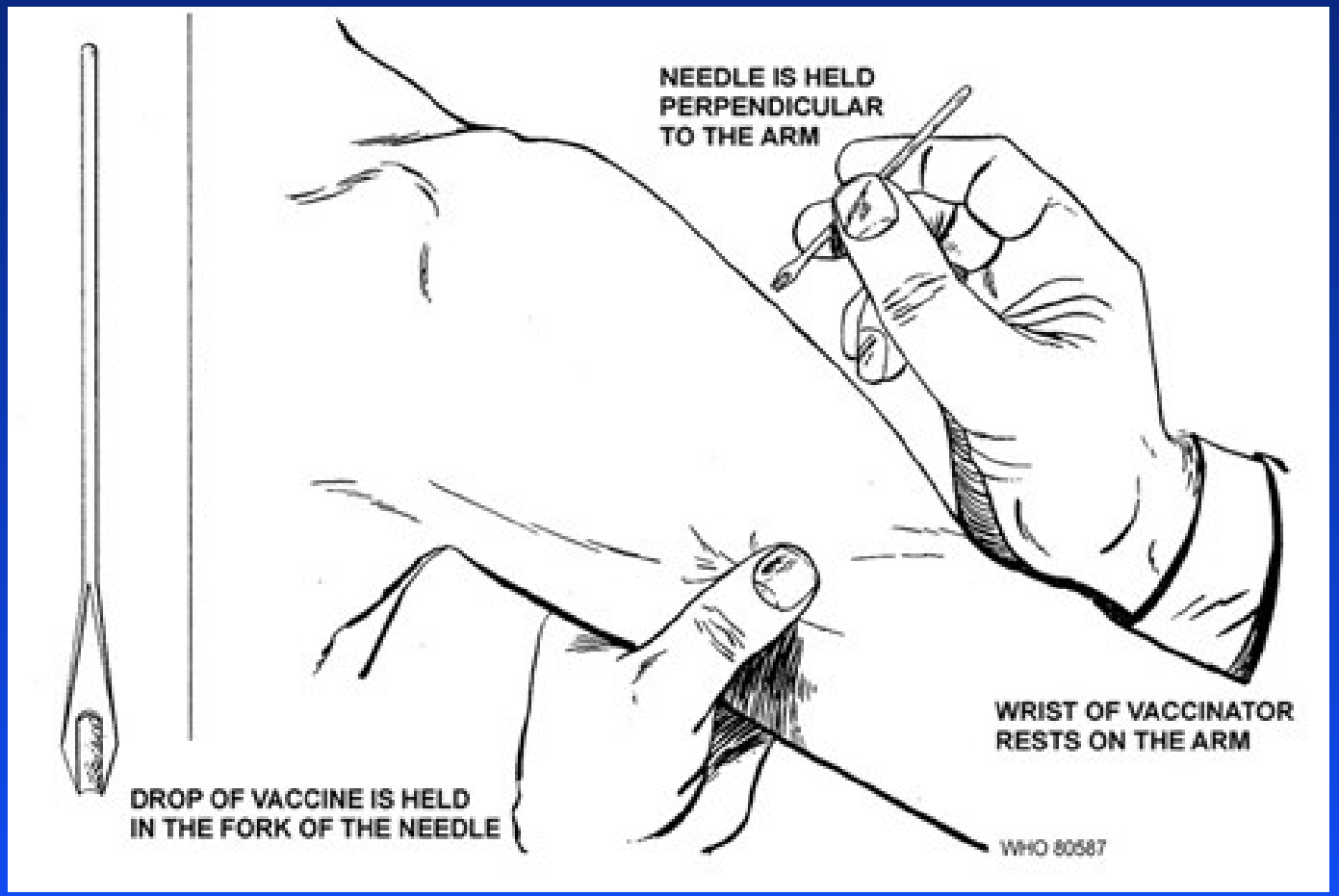
Edward Jenner vaccinating a boy. EE Hillemacher 1884

- **Last case of smallpox in Nigeria - 1970**
- **27 yo ♂ immunized 10 days previously in an area with an ongoing outbreak**
- **Note sparing of trunk and site of immunization**

Vaccinia vaccine

- DoD's use of this vaccine exceeds the remainder of the civilian community
- Fewer problems in DoD population that has been vaccinated than had been anticipated
- Main problem has been variety of rashes that have occurred

Multipuncture vaccination by bifurcated needle



Case Report

- 32 y/o WM has primary smallpox vaccination over left deltoid
- Site covered with semi-permeable dressing
- Vaccination site progresses normally, with exaggerated local reaction

- **Days 11 – 12: peak of local reaction**
- **Develops progressive generalized eruption**
- **Mild (if any) constitutional symptoms without fever**

Clinical Course

- Rash initially maculopapular and intensely pruritic
- Peaks within 48 hours
- One or two isolated (initially) pustular lesions
- Papules rapidly revert to macules
- Rash quickly begins to dissipate
- Fades over next 10 - 14 days

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